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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,637	04/28/2006	Denis Barritault	251867	5413

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EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
08/31/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

Office Action Summary	Application No.	Applicant(s)	
	10/577,637	BARRITAULT ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-9 and 11-16* is/are pending in the application.

4a) Of the above claim(s) *7-9 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments, filed July 6, 2010, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Election/Restrictions

2. Claim 7 – 9 and 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected polymeric species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 17, 2009. In the elected polymer, the Z group is acetate

Terminal Disclaimers

3. The terminal disclaimer filed on July 6, 2010 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent issuing from US Patent Application 10/695574 or the expiration date of US Patent No. 6,689,741 has been reviewed and are accepted. The terminal disclaimer has been recorded.

4. The terminal disclaimer filed on July 6, 2010 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of

any patent to issue from U.S. application 12/213098 has been reviewed and is NOT accepted. The terminal disclaimer does not comply with 37 CFR 1.321(b) and/or (c) because:

> The application/patent being disclaimed has been improperly identified since the incorrect filing date of September 17, 2008 was used. The correct filing date is June 13, 2008.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1 – 9, 12, 14 and 16 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 - 18 of copending Application No. 12/213098.

As discussed above, the terminal disclaimer was not approved so this rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed March 4, 2010.

Specification

7. The amendment filed July 6, 2010 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: as the

abbreviation "FA" was never explained so the definition of this abbreviation to be "fatty acid" at paragraph [0072] introduces new matter into the application. Following the experimental procedure described, it is clear the CMD is carboxymethyldextran. However, in the sulphation protocol, the function or reason for inclusion of "FA" was not stated. It is possible that this ingredient was added in order to introduce Z groups into the polymer, but among the disclosed Z groups are both fatty acids and fatty alcohols (e.g., original claim 10 and presently amended claim 7), both of which could be abbreviated "FA". As the specification as originally filed does not provide sufficient information to conclusively identify what "FA" stands for, the amendment to define this abbreviation as "fatty acid" introduces new matter into the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112 – 1st Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1 – 3, 6, 12, 14 and 16 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. This new matter rejection is MAINTAINED.

Applicants have amended the claims in response to the previously applied new matter rejection. The amended claims still contain new matter as described below. In the specification as originally filed, there is no indication that the substituents X and Y are optionally present in the polymer. Therefore, formulas (Ia) and (Ib) contain new matter as substituents Y and X respectively are not required to be present in each of these formulas. All of the generic disclosure teaches that the intervening group is a requirement so the subject matter disclosed in the specification as originally filed is constrained to those specific polymers without an intervening R group, contrary to the original definition of the Y substituent, are supported. Polymers beyond those explicitly disclosed are within the scope of the amended generic polymer formula (I) and (Ic) so the claims still contain new matter. Additionally, all the explicitly disclosed polymers without such intervening groups contain only glucose monomers. Thus, the glucose monomer A further comprising different monomers selected from the Markush group of claim 2 are new matter.

The limitation wherein "the method [the method of treating pain associated with a tissue] does not treat the condition that causes the pain" is new matter. The specification as originally filed indicates that "the polymers are not intended to treat the various different lesions causing the pain or itching" (¶ [0058] of the specification, emphasis added). This does not provide support for this broad limitation present in the amended claims. As exemplified in dependent claim 12, lesions or irritations are a

subset of the conditions being treated in claim 1. The specification also indicates that in certain cases, treatment resulted in the cure of the disease or lesion which was the cause of the pain (¶ [0054]), including scars (see ¶¶ [0035], [0055]). These disclosures do not provide support for the broad method of treating pain associated with a tissue in which the condition causing the pain is not treated.

10. Claims 1 – 3, 6 and 12 – 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. The specification fails to provide adequate written description for the amounts of biocompatible polymer that treat pain but that results in a the method not treating the condition that causes the pain and how those amounts may or may not vary based on the particular condition that is causing the pain.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1 – 3, 6 and 12 – 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention. The claims have been amended so that while the method treats pain associated with a tissue but the method does not treat the condition that causes the pain. Dependent claims 12 – 16 recite various causes of pain. It is unclear at what level of underlying condition is or is not being treated. For example, claim 16 recites peripheral and/or degenerative neuropathy, and diabetic neuropathy is treated in the specification. In the treatment of diabetic neuropathy is the underlying condition not being treating diabetes and/or the neuropathy caused by diabetes? Scars are also exemplified in claim 16 and the specification indicates that not only is the pain associated with scarring treated by application of the polymer but also that the scar is remodeled, thus treating the condition that causes the pain. It is unclear if a different dosage of polymer can treat the pain without treating the condition causing the pain or if scars and cicatricial tissue pain no longer falls within the scope of amended claim 1. Thus it is unclear if all of the exemplified conditions can be treated as required by amended claim 1 though variation of the dosage or if some of the exemplified compositions describe in the specification no longer fall within the scope of amended claim 1. Please clarify.

Response to Arguments

13. Applicant's arguments with respect to the rejections of the pending claims under 35 U.S.C. 102(b) and 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1 – 3, 6 and 12 – 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barritault et al. (US 20010021758) in view of Vergnolle et al. (TIPS, 2001).

Barritault et al. discloses polymers of formula AaXxYy, wherein A is a monomer, X is a -R-COO-R' wherein R is a bond and R' is a hydrogen atom or cation; Y is a –R-O-SO_3-R' or –R-N-SO_3-R' wherein R is a bond and R' is a hydrogen atom or a cation, x is the substitution rate of the monomers A by group X, which is comprised of approximately 20% and 150%; and y is the substitution rate of monomers A by group Y which is comprised of approximately 30% and 150% (¶¶ [0039] – [0046]). Specific polymers in which A is a glucose monomer on which X, Y and optional substituent Z are grafted on the hydroxyl functions of the glucose monomer (¶ [0187]) are also disclosed. X is $–CH_2COOH$ or $–CH_2COO^-Na^+$, which reads on the X substituent of the instant claims (¶ [0188]). Y is $–OSO_3H$ or $SO_3^-Na^+$, which reads on the O-sulphonate Y substituent of the instant claims (¶ [01890]). Such polymers with different degrees of carboxylmethylation and sulphonation are set forth in the table of figure 6. The polymers may be substituted with various groups Z such as those which are capable of conferring supplementary biological or physicochemical properties, such as better solubility or lipophilic properties enabling better diffusion or tissue penetration, increasing amphiphilic properties, such as amino acids, fatty acids, fatty alcohols, ceramides or nucleotide addressing sequences (¶ [0057]). z, the substitution rate of the A monomers with groups Z are comprised between approximately 0 an 50%, preferably on the order of 30% (¶ [0059]). The invention pertains to the pharmaceutical compositions of the

polymers which are contacted with tissue (¶ [0126]) by routes such as topical administration (¶ [0083]). The polymers have several different properties, including inhibition of protease activities implicated in the inflammatory process (¶ [0067]).

Barritault et al. does not describe the treatment of pain associated with a tissue wherein the method does not treat the condition that causes the pain.

Vergnolle et al. discloses that all of the classical "hallmarks" of inflammation (pain, swelling, redness, heat and impaired function) have been observed following *in vivo* activations of PARs (protease-activated receptors) (p 147, col 1, p 2). Sensory afferent neurons have functional PARs, suggesting that activation of PAR1 or PAR2 could lead to central transmission of a signal (p 150, col 1, ¶ 2). Studies have demonstrated that PAR2 contributes to the central transmission of nociceptive messages and the induction of hyperalgesia (p 150, col 1, ¶ 2). PAR2 might have a role in both somatic pain and visceral hypealgesia (p 150, col 1, ¶ 2). These receptors activate a nocicpetive pathway, suggesting a role for proteases in pain transmission and making them a potential therapeutic target for inflammation and pain (p 150, col 2, ¶ 1).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the polymers of Barritault et al that inhibit protease activities implicated in the inflammatory process in a method of treating pain wherein only the pain and not the underlying condition is treated. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Barritault et al. discloses that the claimed polymers inhibit protease activities implicated in inflammatory process and Vergnolle et al. discloses that

the protease-activated receptor PAR2 whose activation leads to the hallmarks of inflammation, mediates a nociceptive pain response. Application of the polymer with inflammatory associated protease inhibitory activity would then prevent activation of PAR2, treating the pain. The blocking of the generation and/or transmission of the pain response from activated PAR2 would treat the pain but not the underlying cause of the pain. The inflammation response is a general response to pain induced by lesions or irritation of an area in contact with an outside medium,

Barritault et al. discloses that the polymers can be administered by a variety or routes, including topical. The selection of the appropriate administration route is within the skill of one of ordinary skill in the art based on the condition being treated. For example, pain in a joint or associated with a cut, ulcer or other skin lesion can easily be treated by topical application of the polymer. Blocking of the sensory afferent neuron will not result in treatment of the condition causing the pain.

18. Claims 1 – 3, 6 and 12 – 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barritault et al. and Vergnolle et al. as applied to claims 1 – 3, 6 and 12 – 16 above, and further in view of Deibig et al. (US 4,451,452).

As discussed in greater detail above, Barritault et al. and Vergnolle et al. teach the treatment of pain without treatment of the cause of the pain, using polymers according to formula (I), because these polymers inhibit protease activities implicated in the inflammation process. The polymers may be substituted with various groups Z such as which are capable of conferring supplementary biological or physicochemical

properties, such as better solubility or lipophilic properties enabling better diffusion or tissue penetration, increasing amphiphilic properties, such as amino acids, fatty acids, fatty alcohols, ceramides or nucleotide addressing sequences (p [0057]). z, the substitution rate of the A monomers with groups Z are comprised between approximately 0 an 50%, preferably on the order of 30% (¶ [0059]).

Barritault et al. does not disclose polymers substituted with acetate groups as Z.

Deibig et al. discloses the modification of the physical properties of water-soluble polymers such as dextran by incomplete esterification with mono- or di-carboxylic acid that make the polymers water-insoluble but still water-swellable (abstract). The selection of the polymeric hydroxy compound, the acylating group and the degree of acylation enables a wide range of polymers of different properties and hydrolysis rates to be prepared (col 1, ln 27 – 20). In example 4, dextran acetate is prepared (col 5, ln 19 – 43). As shown in table I (col 6), increasing the degree of substitution of a larger carboxylic acid side chain, butyrate, on dextran decreased the amount of water uptake (swellability) of the polymer.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the carboxymethylated and O-sulphonated biocompatible polymers of Barritault et al. with acetate groups. The person of ordinary skill in the art would have been motivated to make those modifications to alter the swellability and solubility properties of the resulting polymers and reasonably would have expected success because Deibig disclose that substitution of dextran with carboxylic acids such as acetate affects the physical properties of the final polymers,

allowing for polymers with a wide variety of final characteristics based on the identity and degree of substitution of the polymer.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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